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10/502,059	08/02/2004	Bernd Stahl	STAH3007/REF	4218

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EXAMINER	
LAU, JONATHAN S	

ART UNIT	PAPER NUMBER
1623	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/502,059	STAHL ET AL.	
	Examiner	Art Unit	
	Jonathan S. Lau	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 June 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *56-75* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *56-75* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is responsive to Applicant's Amendment and Remarks, filed 1 Jun 2010, in which claim 56 is amended to change the scope and breadth of the claim and claims 64 and 69 are amended to conform to the language of amended claim 56.

This application is the 371 national stage entry of PCT/EP03/00505, filed 20 January 2003, claiming benefit of foreign priority document Germany 102 03 999.2, filed 1 February 2002. An English language translation of this foreign priority document is not of record.

Claims 56-75 are pending in the instant application and examined on the merits herein.

Objections Withdrawn

Applicant's Amendment, filed 1 Jun 2010, with respect to objections to claim 56 has been fully considered and is persuasive, as amended claim 56 does not recite the detailed informalities.

This objection has been **withdrawn**.

Rejections Withdrawn

Applicant's Amendment, filed 1 Jun 2010, with respect to claims 56-63, 65-68, 70-72 and 75 rejected under 35 U.S.C. 102(b) as being anticipated by Hirai et al. (US

Patent 4,616,008, issued 7 Oct 1986, of record) has been fully considered and is persuasive, as amended claim 56 requires the composition does not comprise and anti-infective active agent other than said cycloglycans and Hirai et al. requires a cephalosporin antibiotic.

This rejection has been **withdrawn**.

Applicant's Amendment, filed 1 Jun 2010, with respect to claims 56-72 and 75 rejected under 35 U.S.C. 103(a) as being unpatentable over Hirai et al. (US Patent 4,616,008, issued 7 Oct 1986, of record) has been fully considered and is persuasive, as amended claim 56 requires the composition does not comprise and anti-infective active agent other than said cycloglycans and Hirai et al. requires a cephalosporin antibiotic.

This rejection has been **withdrawn**.

Applicant's Amendment, filed 1 Jun 2010, with respect to claims 73 and 74 rejected under 35 U.S.C. 103(a) as being unpatentable over Hirai et al. (US Patent 4,616,008, issued 7 Oct 1986, of record) as applied to claims 56-72 and 75 above, in view of Thornsberry (Clinical Infectious Diseases, 1992, 14(2), pS189-S196, of record) has been fully considered and is persuasive, as amended claim 56 requires the composition does not comprise and anti-infective active agent other than said cycloglycans and Hirai et al. requires a cephalosporin antibiotic and Thornsberry does not remedy the teachings of Hirai.

This rejection has been **withdrawn**.

Duplicate Claims

Applicant is advised that should claim 66 be found allowable, claim 71 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Both claims 66 and claim 71 depend from claim 60 and appear to recite duplicate limitations.

The following are new grounds of rejection necessitated by Applicant's Amendment, filed 1 Jun 2010, in which claim 56 is amended to change the scope and breadth of the claim. Claims 57-75 depend from claim 56 and incorporate all limitations therein.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Amended Claims 56-75 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roth et al. (WIPO publication WO/90/00596, provided by Applicant on IDS filed 2 August 2004) in view of Hildreth (US Patent Application Publication 2002/0128227, published 12 Sep 2002, filed 8 Mar 2001, cited in PTO-892) and further in view of Shin et al. (Microbes and Infection, 2001, 3, p755-761, cited in PTO-892), Norkin (Advanced Drug Delivery Reviews, 2001, 49, p301-315, cited in PTO-892) and Duncan et al. (Cellular Microbiology, 2002, 4(12), p783-791, cited in PTO-892).

Roth et al. teaches using a carbohydrate to block cell to cell transmission of a virus, HIV (page 9, lines 15-19). Roth et al. teaches the use of α-, β-, and γ-CD, possibly derivatized at the C-2, 3, and 6 OH groups of the constituent sugars of the CD (page 10, lines 7-10 and 17-19). Cyclodextrin is a cycloglycan composed of 6 (α-CD), 7 (β-CD), or 8 (γ-CD) glucose units linked by α(1-4) glycosidic bonds (definition of cyclodextrin, The Merck Index, of record). Roth et al. teaches administering an amount to result in interference with binding of the virus with the cells (page 14, lines 10-30). Roth et al. teaches the embodiments of β-CD, β-CD with 4 sulfate groups, β-CD with 4 propoxy groups, and β-CD with 14 sulfate groups (page 24, lines 24-29). Roth et al. teaches the

administration of the carbohydrate to cells within the body of a mammal including humans by several routes of administration, for example the oral route (page 15, lines 15-21). Roth et al. teaches the cyclodextrin operates early in the viral attack on the cell and exert their effects at the cell membrane during the initial phases of attack on the cell (page 28, lines 20-25 and page 29, lines 15-20).

Roth et al. does not specifically teach the method for reducing the invasion and infection of mammalian cells by pathogenic intracellular bacteria selected from the group consisting of *E. coli*, *Listeria* and *Salmonella* (instant claims 56, 72, 73 and 74). Roth et al. does not specifically teach the method wherein the inert carrier that said cycloglycan may be bound to is a peptide, protein, lipid, lipoid, polymer or biopolymer (instant claims 61, 66 and 71). Roth et al. does not specifically teach the method wherein the composition is administered with a probe to the stomach of a human subject (instant claims 62 and 67). Roth et al. does not specifically teach the method wherein the composition is a pharmaceutical composition (instant claims 63 and 68). Roth et al. does not specifically teach the method wherein the composition is administered once daily in an amount of at least 1 mg cycloglycan per kg body weight to a human subject (instant claims 64 and 69). Roth et al. does not specifically teach the method wherein the mammalian cells are in the GI tract, blood system, respiratory passages, urogenital tract or nasopharynx of a human subject (instant claims 65 and 70). Roth et al. does not specifically teach the method wherein the subject is a pregnant woman, sick person, debilitated person, or elderly person (instant claim 75).

Hildreth teaches a method of reducing risk of transmission of sexually transmitted pathogens comprising a topical administration contacting the pathogen or cells with a β-cyclodextrin, where the pathogens are viral or bacterial (page 1, paragraph 11). Hildreth teaches the use of β-CD and hydroxyproyl-β-CD (page 2, paragraphs 17 and 18), or β-CD with propoxy groups. Hildreth teaches the β-CD operates by affecting lipid rafts to reduce cellular invasion by said pathogens (page 3, paragraphs 24 and 25). Hildreth teaches the broader field of the invention is agents and methods for preventing a viral or microbial infection (page 1, paragraph 4). Hildreth teaches teach the subject is a mammal and preferably a human (page 9, paragraph 59 at top left). Hildreth teaches it is within the level ordinary skill in the art to formulate a composition administered to a human into a pharmaceutically composition and teaches pharmaceutically acceptable excipients and carriers include polymers such as the proteins gelatin or keratin, or starch, which are polymers and biopolymers, and triglycerides, a lipid (page 9, paragraphs 63- 64). Hildreth teaches the β-CD administered at about 0.1 to 2 grams (page 10, paragraph 67), or about 1.67 to 33 mg/kg assuming the average 60 kg human.

Shin et al. teaches pathogens such as bacteria, bacterial toxins, viruses and parasites are known to be capable of entry into host cells via caveolae or lipid rafts (page 755, abstract and left column). Shin et al. teaches the pathogens, varying widely in size and other traits, share the capacity to utilize the same caveolar machinery and endocytic pathway (paragraph spanning page 755 and 756). Shin et al. teaches microbes known to utilize caveolae or lipid rafts for entry into host cells include the virus

HIV and the bacteria *E. coli* (page 756, table 1 at top of page). Shin et al. teaches *E. coli* is an opportunist pathogen causing extraintestinal infections in elderly and immuno-compromised patients (page 757, left column, paragraph 2). Shin et al. teaches methyl β-CD is shown to block uptake of *E. coli* and disrupt caveolae (page 757, right column, paragraph 3).

Norkin teaches a variety of pathogens, including viruses, intracellular bacteria, and prions, as well as certain bacterial toxins, are known to enter cells via caveolae (page 301, abstract). Norkin teaches said pathogens include HIV (page 307, left column section 2.6), and bacteria such as *Listeria monocytogenes, Salmonella* (page 308, left column, paragraph 1) and *E. coli* (page 308, right column, section 3.2). Norkin teaches *E. coli* is responsible for mild to severe opportunistic infections of the digestive and urinary tracts (page 308, right column, paragraph 3) and teaches the methyl β-CD is shown to block uptake of *E. coli* and disrupt caveolae (page 309, left column, paragraph 2) as taught by Shin et al.

Duncan teaches pathogens are known to enter cells via caveolae and lipid rafts (page 783, Summary at left column). Duncan teaches a wide range of microbes use the same endocytic pathway to gain entry to host cells (paragraph spanning page 783, right column and page 784, left column). Duncan teaches bacteria such as *Listeria monocytogenes, Salmonella typhimurium* (page 787, right column, paragraph 1-2) and *E. coli* whose entry is inhibited by methyl β-CD (page 787, right column, paragraph 3).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine Roth et al. in view of Hildreth and in view of Shin et al., Norkin and

Duncan et al. One of ordinary skill in the art would have been motivated to combine Roth et al. in view of Hildreth and in view of Shin et al., Norkin and Duncan et al. to apply the method of Roth et al. to pathogens other than HIV because Hildreth teaches the topical use of β-CDs to reduce cellular invasion by both HIV viral and bacterial pathogens, Shin et al., Norkin and Duncan et al. teach a variety of pathogens, including the virus HIV and intracellular bacteria, are known to enter cells via caveolae of the same endocytic pathway and identify bacteria such as *Listeria, Salmonella* and *E coli* as said pathogens, and it is the motivation of one of ordinary skill in the art to treat said disease-causing pathogens. One of ordinary skill in the art would have had a reasonable expectation of success to combine the oral administration of Roth et al. in view of the topical administration of Hildreth because both Roth et al. and Hildreth teach the route of administration is effective to reduce HIV infection and Hildreth suggests that one of ordinary skill in the art at the time of the invention has a reasonable expectation of success for administration of β-CD via the same route of administration to treat both viral and bacterial pathogens with some degree of predictability. See also MPEP 2143.02. One of ordinary skill in the art would have had a reasonable expectation of success to combine Roth et al. in view of Hildreth and in view of Shin et al., Norkin and Duncan et al. to apply the method of Roth et al. to pathogens other than HIV because Shin et al., Norkin and Duncan et al. teach the variety of pathogens including HIV and bacteria are known to enter cells via caveolae of the same endocytic pathway and teach methyl β-CD to inhibit *E. coli* entry. It would have been obvious to one of ordinary skill in the art that the common pharmaceutically acceptable excipients and carriers taught by

Hildreth are applicable to oral dosage forms taught by Roth et al. The common pharmaceutically acceptable excipients taught by Hildreth are interpreted as a type of "probe" in that they explore or investigate whether the composition was administered to the subject.

The declaration of inventor Bernd Stahl of record, previously filed 2 Feb 2009, has been considered and not found to be persuasive. The newly cited Shin et al., Norkin and Duncan et al. suggest that one of ordinary skill in the art at the time of the invention understood a variety of pathogens, including the virus HIV and intracellular bacteria such as *Listeria, Salmonella* and *E coli*, are known to enter cells via caveolae of the same endocytic pathway and that methyl β-CD is expected inhibit *E. coli* entry by disruption of said caveolae.

Conclusion

No claim is found to be allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jonathan S. Lau whose telephone number is 571-270-3531. The examiner can normally be reached on Monday - Thursday, 9 am - 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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